Please add new claim 29 as follows:

29. (new) The method of claim 1 which further comprises steps a), b) and c) one or more times.

Please add new claim 30 as follows:

30. (new) The method of claim 14 wherein one of the restriction enzyme specific primers is tagged.

Remarks

Claims 1-28 are pending in the instant application. Applicants have amended claims 1, 2, 6, 7, 9, 10, 11, 15, 16, 17, 21, 22, 23, and 28 to more fully conform with U.S. practice and to delete multiple dependencies. Applicants have cancelled, without prejudice, claims 3, 12, 13, 19, 20, and 26. Applicants have also added new claims 29 and 30. A version of the claims marked up to show the amendments, as well as a clean version of the claims encompassing the amendments, is attached hereto.

Applicants respectfully assert that all amendments are fairly based on the specification, and respectfully request their entry.

Applicants believe that the claims, as amended, are in allowable form, and earnestly solicit the allowance of claims 1, 2, 4-11, 14-18, 21-25, and 27-30.

Respectfully submitted,

Royal N. Ronning, Jr. 32,529
Attorney for Applicants

Amersham Pharmacia Biotech, Inc.
800 Centennial Avenue
P. O. Box 1327
Piscataway, New Jersey 08855-1327

Tel: (732) 457-8423
Fax: (732) 457-8463

H:\DEPT\Law_Dept\IP Dept\Amendments\First Preliminary Amendment-PA9912 (8-28-01).doc

Claims (marked-up version showing amendment(s))

[CLAIMS]

What is claimed is:

1. (once amended) [A]In a method of providing a mixture of DNA fragments enriched in fragments that are characteristic of a phenotype of interest, [by]which method includes providing affected DNA in fragmented form and providing unaffected DNA in fragmented form, [which method comprises]the improvement comprising:

   a) mixing the fragments of the affected DNA and the fragments of the unaffected DNA under hybridising conditions to form hybrids;

   b) recovering a mixture of hybrids that contain mismatches;

   c) recovering fragments of the affected DNA from the mixture of hybrids that contain mismatches[;

   and optionally repeating steps a), b) and c) one or more times].

2. (once amended) The method of claim 1 wherein the affected DNA is pooled DNA of one or more individuals who show the phenotype of interest, and the unaffected DNA is pooled DNA of one or more individuals who do not show the phenotype of interest.

6. (once amended) The method of [any one of claims 1 to 5]claim 1, wherein step b) is performed by use of a mismatch-binding protein.

7. (once amended) The method of [any one of claims 1 to 6]claim 1, wherein either the fragments of the affected DNA or the fragments of the unaffected DNA are tagged by one member of a specific binding pair, and step c) is performed by using the other member of the specific binding pair.

9. (once amended) The method of [any one of claims 1 to 8]claim 1, [wherein]further comprising subjecting the mixture of DNA fragments enriched in fragments that are characteristic of the phenotype of interest[, is subjected] to self-hybridisation [followed by recovery of]to form duplexes and subsequently recovering the perfectly matched duplexes.

10. (once amended) The method of [any one of claims 1 to 9]claim 1, [wherein]further comprising mixing the mixture of DNA fragments enriched in fragments that are characteristic of the phenotype of interest[, is mixed] with an excess of the fragments of the affected DNA under hybridisation conditions[,] to form duplexes and subsequently recovering the[followed by recovery of] perfectly matched duplexes.

11. (once amended) The method of [any one of claims 1 to 10]claim 1, wherein each of the affected DNA and the unaffected DNA is provided in fragmented form by digestion with from 4 to 7 six-cutter restriction endonuclease enzymes together with from 0 to 50 four-cutter restriction endonuclease enzymes.

15. (once amended) The method of [claim 13 or]claim 14, wherein steps a to f) are repeated using each different subset of r restriction endonuclease enzymes to give (n!)/[(n-r)!r!] different arrays.

16. (once amended) The method of [any one of claims 13 to 15]claim 14, wherein the n restriction endonuclease enzymes are selected from 4-cutters and 5-cutters and 6-cutters.

17. (once amended) The method of [any one of claims 13 to 16]claim 14, wherein the n is 3 to 10 and r is 2 to 4.

21. (once amended) [The]A set of arrays [of claim 19 or claim 20]produced by the method of claim 14, derived from a set of n = 6 six-cutter restriction endonuclease enzymes which are *BamHI*; *Bsr GI*; *Hind III*; *Ncol*; *Spel*; and *AflII*.

22. (once amended) [The]A set of arrays [of claim 19 or claim 20]produced by the

method of claim 14, derived from the set of n = 6 six-cutter restriction endonuclease enzymes which are *EcoRI*; *BspHI*; *BglII*; *Xbal*; *Acc65I*; and *ApaLI*.

23. (once amended) A nucleic acid characterisation method which comprises presenting to [the]a set of arrays [of any one of claims 19 to 22]produced by the method of claim 14 a nucleic acid fragment of interest under hybridisation conditions, and observing a pattern of hybridisation.

28. (once amended) The double-stranded DNA molecule of claim 27, wherein[the following criteria are satisfied]:

a) inter-fragment length differences are greater for larger fragments;

b) all possible fragments are unambiguously resolvable by electrophoresis from one another;

c) size gaps between bands comprising different numbers of inter-restriction-site units are larger than size gaps between bands comprising the same number of inter-restriction-site units;

d) the size gaps and size spread from the largest to the smallest fragment are electrophorectically compatible.

29. (new) The method of claim 1 which further comprises steps a), b) and c) one or more times.

30. (new) The method of claim 14 wherein one of the restriction enzyme specific primers is tagged.